

REMARKS/ARGUMENTS

Status of Claims

Claims 1-10, 19, 31-45, 47, 50-52, 55-68, 85-87, 112-121 and 151-157 are pending in the application.

Claims 8, 19 and 157 are withdrawn from consideration.

Claims 9, 37, 41 and 151 have been canceled.

Claims 1-7, 10, 31-36, 38-40, 42-44, 45, 52, 61, 66-67, 86-87, 112-117, 120-121 and 152-155 are currently amended for various reasons as described below.

Claim 1 has been amended to replace the language "a delivery vehicle" to "a delivery vehicle comprising a liposome, wherein said liposome is a positively charged liposome; a negatively charged liposome; or a neutral liposome. Support for this amendment can be found within the existing claim language and throughout the specification as filed and specifically at least in paragraphs [0024], [0026] and [0051]-[0059].

The method of claim 1 has been further amended to read administering to a subject "with cancer". Support for this amendment can be found within the existing claim language and throughout the specification, and specifically at least in paragraphs [0142], [0147] and [0148].

Claims 2 and 5 have been amended to remove the language related to "a ligand for a" pattern recognition receptor to "said pattern recognition receptor" based on the antecedence of claim 1. Support for this amendment can be found within the existing claim language and throughout the specification as filed.

Claim 3 has been amended to better clarify the lists of signaling pattern recognition receptors and Tool-like receptors. Support for this amendment can be found within the existing claim language and throughout the specification, and specifically at least in paragraphs [0020], and [0024].

Claim 4 has been amended to replace the language "ligand" with "signaling pattern recognition receptor". Support for this amendment can be found within the existing

claim language and throughout the specification, and specifically at least in paragraphs [0020], and [0024].

Claim 6 has been amended to replace the language "further comprising modulating" with "wherein said administering step modulates". Support for this amendment can be found within the existing claim language and throughout the specification, and specifically at least in paragraphs [0047], [0048] and [0140].

Claims 7 and 32 have been amended to replace the language "an" with "said" immune response. Support for this amendment can be found within the existing claim language and throughout the specification as filed.

Claim 10 has been amended to change the dependency from canceled claim 9 to amended claim 1; and to clarify the language relating to the cancers claimed. The claim has been amended to include the language "said" cancer comprises one or more "cancers" selected from "the group consisting of." Support for this amendment can be found within the existing claim language and throughout the specification, and specifically at least in paragraphs [0141], [0145] and [0147].

Claim 31 has been rewritten as an independent claim instead of a dependent claim from claim 1. The preamble has been amended to replace the language "The method of claim 1 wherein said composition comprises" to "A method of inducing an immune response in a subject with cancer and exposed to radiation comprising:" Support for this amendment can be found within the existing claim language and throughout the specification, and specifically at least in paragraphs [0141], [0145] and [0147].

Further, claim 31 has been amended to replace the language "a ligand for the pattern recognition molecule family" to "administering to said subject a composition comprising a ligand for a pattern recognition molecule family". Support for this amendment can be found within the existing claim language and throughout the specification, and specifically at least in paragraphs [0049], [0070] and [0156].

Additionally claim 31 has been amended to replace the language "a delivery vehicle" to "a delivery vehicle comprising a liposome, wherein said liposome is a positively charged liposome; a negatively charged liposome; or a neutral liposome." Support for this

amendment can be found within the existing claim language and throughout the specification as filed and specifically at least in paragraphs [0024], [0026] and [0051]-[0059].

Finally, claim 31 has been amended to replace the language "said composition is capable of inducing an immune response in a subject" to "wherein administering said composition induces said immune response in said subject." Support for this amendment can be found within the existing claim language and throughout the specification as filed.

Claim 33 has been amended to delete the term "an innate immune response" to "a response". And changes "by macrophages, neutrophils, NK cells, and/or dendritic cells" to read "by macrophages, neutrophils, natural killer (NK) cells, or dendritic cells, or any combination thereof." Support for this amendment can be found within the existing claim language and throughout the specification, and specifically at least in paragraphs [0049], [0066] and [0104].

Claim 34 has been amended to change the language "the delivery vehicle" to "said liposome" and amends the "liposome" to comprise a "charged liposome." Support for this amendment can be found within the existing claim language and throughout the specification, and specifically at least in paragraphs [0026], [0051] and [0052].

Claims 35, 36, 40 and 52 have been amended to change the dependency from claim 34 to claim 31. Support for this amendment can be found within the existing claim language and throughout the specification as filed.

Claim 38 has been amended to change the language "delivery vehicle comprises any combination of liposomes" to "liposome comprises a neutral liposome." Support for this amendment can be found within the existing claim language and throughout the specification, and specifically at least in paragraphs [0024], [0026] and [0051]-[0059].

Claim 39 has been amended to replace the language "a" with "said" ligand. Support for this amendment can be found within the existing claim language and throughout the specification as filed.

Claim 42 has been amended to change the dependency from claim 41 to claim 31; and amend the language "the non-liposomal delivery vehicle comprises at least one vehicle selected from" to "the delivery vehicle further comprises at least one component selected from the group consisting of:" Support for this amendment can be found within the existing claim

language and throughout the specification, and specifically at least in paragraphs [0026], [0181] and [205].

Claim 43 has been amended to replace the language "TLR" with "toll-like receptor(TLR)" ligand. Support for this amendment can be found within the existing claim language and throughout the specification as filed.

Claim 45 has been amended to change the dependency from claim 44 to claim 43; and amend the language "said nucleic acid molecule is from a bacterium" to "said TLR ligand comprises a nucleic acid molecule from a bacterium." Support for this amendment can be found within the existing claim language and throughout the specification, and specifically at least in paragraphs [0024], [0050] and [0071].

Claim 61 has been amended to replace the language "at least one molecule selected from bacterial DNA, eukaryotic DNA, dsDNA, ssDNA a synthetic oligonucleotide, RNA, and synthetic RNA" to read "at least one molecule selected from the group consisting of: eukaryotic DNA, eukaryotic dsDNA, eukaryotic ssDNA, a synthetic oligonucleotide, eukaryotic RNA, and synthetic RNA." Support for this amendment can be found within the existing claim language and throughout the specification, and specifically at least in paragraphs [0049], [0059] and [0156].

Claim 66 has been amended to replace the language "further comprising a molecule" with "wherein said composition further comprises a molecule." Support for this amendment can be found within the existing claim language and throughout the specification as filed.

Claim 67 has been amended to replace the language "further comprising a DNA condensing agent" with "wherein said composition further comprises a DNA condensing agent." Support for this amendment can be found within the existing claim language and throughout the specification as filed.

Claim 86 has been amended to replace the language "in a subject disposed of cancer" with "in a subject having cancer." Support for this amendment can be found within the existing claim language and throughout the specification, and specifically at least in paragraphs [0142], [0147] and [0148].

Claim 87 has been amended to replace the language "one cancer selected from" to "one cancer selected from the group consisting of." Support for this amendment can be found within the existing claim language and throughout the specification as filed and specifically at least in paragraphs [0142], [0147] and [0148].

Claim 112 has been amended to replace the language "a method of treating a subject with cancer" to "a method of treating a cancer in a subject in need of treatment for said cancer". Support for this amendment can be found within the existing claim language and throughout the specification as filed and specifically at least in paragraphs [0142], [0147] and [0148].

Additionally claim 112 has been amended to replace the language "a delivery vehicle" to "a delivery vehicle comprising a liposome, wherein said liposome is a positively charged liposome; a negatively charged liposome; or a neutral liposome. Support for this amendment can be found within the existing claim language and throughout the specification as filed and specifically at least in paragraphs [0024], [0026] and [0051]-[0059].

Further, claim 112 has been amended to replace the language "method elicits a response in a subject disposed of cancer" with "composition elicits an immune response in said subject, thereby treating said cancer in said subject." Support for this amendment can be found within the existing claim language and throughout the specification as filed and specifically at least in paragraphs [0147], [0148] and [0163].

Claim 113 has been amended to replace the language "comprising at least one therapy consisting of" with "comprising administering at least one additional therapy selected from the group consisting of:". Support for this amendment can be found within the existing claim language and throughout the specification as filed and specifically at least in paragraphs [0141] and [0143].

Claims 114 and 152 have been amended to replace the language "administering the therapy" to "administering the radiation therapy". Support for this amendment can be found within the existing claim language and throughout the specification, and specifically at least in paragraphs [0141], [0142] and [0144].

Claim 115 has been amended to change the dependency from claim 114 to claim 112; and has been amended to replace the language "radiation therapy is introduced first" to "radiation therapy is administered to said subject before administering said composition." Support for this amendment can be found within the existing claim language and throughout the specification, and specifically at least in paragraphs [0141], [0142] and [0144].

Claim 116 has been amended to change the dependency from claim 114 to claim 112; and has been amended to replace the language "radiation therapy is introduced last" to "radiation therapy is administered to said subject after administering said composition." Support for this amendment can be found within the existing claim language and throughout the specification, and specifically at least in paragraphs [0141], [0142] and [0144].

Claim 117 has been amended to change the dependency from claim 114 to claim 112; and has been amended to replace the language "radiation therapy is introduced concurrently" to "radiation therapy is administered to said subject concurrently with the administration of said composition." Support for this amendment can be found within the existing claim language and throughout the specification, and specifically at least in paragraphs [0141], [0142] and [0144].

Claim 120 has been amended to replace the language "a liposome" to "a charged liposome" Support for this amendment can be found within the existing claim language and throughout the specification, and specifically at least in paragraphs [0024], [0026] and [0051]-[0059].

Claim 121 has been amended to replace the language "non-lioposomal delivery vehicle" to "a neutral liposome." Support for this amendment can be found within the existing claim language and throughout the specification, and specifically at least in paragraphs [0024], [0026] and [0051]-[0059].

Claim 152 has been amended to replace the language "the therapy" to "the radiation therapy." Support for this amendment can be found within the existing claim language and throughout the specification, and specifically at least in paragraphs [0141], [0142] and [0144].

Claim 153 has been amended to change the dependency from claim 152 to claim 1; and has been amended to replace the language "wherein radiation exposure occurs first" to "wherein the radiation is administered before said composition." Support for this amendment can be found within the existing claim language and throughout the specification, and specifically at least in paragraphs [0141], [0142] and [0144].

Claim 154 has been amended to change the dependency from claim 152 to claim 1; and has been amended to replace the language "wherein radiation exposure occurs last" to "wherein the radiation is administered after said composition." Support for this amendment can be found within the existing claim language and throughout the specification, and specifically at least in paragraphs [0141], [0142] and [0144].

Claim 155 has been amended to change the dependency from claim 152 to claim 1; and has been amended to replace the language "wherein radiation exposure is concurrent with said administering" to "wherein the radiation is administered concurrently with said composition." Support for this amendment can be found within the existing claim language and throughout the specification, and specifically at least in paragraphs [0141], [0142] and [0144].

No acquiescence is made to any position regarding patentability as set forth in the Office Action mailed May 17, 2007. Applicants reserve the right to pursue the subject matter no longer within the scope of the amended claims in a continuing application without prejudice.

No new matter has been introduced. Entry of the above revisions is respectfully requested.

1) Elections/Restrictions

Applicants thank the Examiner for recognizing that should the species claims be found allowable the linking claims subject to previous restriction will also be found allowable.

2) Claims to Non-elected Inventions

Claims 8, 19, and 157 were allegedly drawn to non-elected inventions and withdrawn from consideration.

3) Claim Rejections under 35 USC §112, second paragraph

Claims 6, 7, 9, 31-45, 47, 50-52, 55-68, 112-121, 151, and 152 were rejected under 35 USC §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. After reviewing the rejections, Applicants respectfully traverse; however for business considerations and in an effort to expedite prosecution the claims have been addressed as follows:

Claim 6 was found indefinite because it is allegedly not clear if the phrase "further comprising modulating an immune response in said subject" is a reference to the effect of performing the method of claim 1, or if this refers to an additional active step. The Examiner has suggested the "the claim would be clear if it contained a step of administering another product or composition." Claim 6 has been amended to replace the allegedly indefinite term "further comprising modulating" with "wherein said administering step modulates." In light of the amendment this rejection should be withdrawn.

Claim 7 is dependent from claim 6 and the rejection should be withdrawn in light of the amendment to claim 6 described above.

Claim 9 has been canceled thus rendering the rejection moot.

Claim 31 was found indefinite because the phrase "is capable of inducing an immune response in a subject" is allegedly unclear. The language in claim 31 has been amended to "induces said immune response in said subject."

In light of the above amendment to claim 31 the rejection should be withdrawn.

Furthermore claims 32-36 are dependent from claim 31 and were rejected on the same basis as claim 31; therefore in light of the above amendment to claim 31, the rejections should be withdrawn for dependent claims 32-36.

Claim 37 has been canceled thus rendering the rejection moot.

Claim 38 was found indefinite because allegedly in the phrase "any combination of liposomes" it is not clear whether this refers to liposomes made of different lipids, or comprising different drugs. Furthermore, there was no antecedent basis for the concept of different types of liposomes in claim 31, from which claim 38 depends. Claim 38 has been amended to now read "wherein said liposome comprises a neutral liposome."

In light of the amendment to claim 31 the rejection should be withdrawn.

Furthermore claims 39-40, 42-45, 47, 50-52, 55-65 are dependent from claim 31 and were rejected on the same basis as claim 31; therefore in light of the above amendment to claim 31, the rejections should be withdrawn for dependent claims 39-40, 42-45, 47, 50-52, 55-65.

Claim 41 has been canceled therefore the rejection is moot.

Claim 66 was found indefinite because although the claim is dependent from claim 31, which is a claim to a method. The phrase "further comprising a steroid backbone" is a limitation that would be appropriate for a claim to a composition or a product. The claim has been amended to clarify this relationship and now reads "wherein said composition further comprises a molecule with a steroid backbone."

In light of the amendment to claim 66 the rejection should be withdrawn.

Claim 67 was found indefinite because the claim is dependent from claim 60, which is a claim to a method, the phrase "further comprising a DNA condensing agent" is a limitation that would be appropriate for a claim to a composition or a product. The claim has been amended to clarify this relationship and now reads "wherein said composition further comprises a DNA condensing agent."

In light of the amendment to claim 67 the rejection should be withdrawn.

Claim 68 is dependent from claim 67 and the rejection should be withdrawn in light of the amendment to claim 67 described above.

Claim 112 was found indefinite because the preamble phrase "in a subject disposed of cancer" is allegedly unclear. The language in claim 112 has been amended to read "treating a cancer in a subject in need of treatment for said cancer." Additionally claim 112 was found to be further indefinite allegedly because in the preamble the claims reads "treating a subject with cancer", whereas in the body of the claim, the claim reads "wherein said method elicits a response in a subject disposed of cancer", as stated above the preamble language has been amended; furthermore the body of the claim language has also been amended to read "composition elicits an immune response in said subject, thereby treating said cancer in said subject".

In light of the amendments to claim 112 the rejection should be withdrawn.

Furthermore claims 113-121 are dependent from claim 112 and were rejected on the same basis as claim 112; therefore in light of the above amendment to claim 112 the rejections should be withdrawn for dependent claims 113-121.

Claim 151 has been canceled therefore the rejection is moot.

Claim 152 was found indefinite because of the phrase "the therapy" allegedly lacked antecedent basis. The claim has been amended to read "the radiation therapy" which is introduced in claim 1 from which claim 152 depends.

Therefore in light of the amendments to claim 152 the rejection should be withdrawn.

Based on the amendments and cancellation of the above claims the 35 USC §112, second paragraph rejections should be overcome, and Applicants respectfully ask the Examiner to withdraw the rejection.

4) Claim Rejections under 35 USC §112, first paragraph

Claims 9, 10, 112-121 were rejected under 35 USC §112, first paragraph, because the specification, while being enabling for methods of treating a subject having cancer, does not reasonably provide enablement for methods of preventing cancer in a subject. The basis for this rejection was that the specification allegedly fails to enable one of skill in the art to use the claimed compositions as prophylactic or therapeutic cancer vaccines for the intended use of preventing cancer.

Applicants have reviewed the Examiner's rejection and the specification and respectfully traverses. However, for business considerations and in an attempt to expedite prosecution the claims have been amended such that all the above rejected claims now read on methods of treating a subject having cancer.

In light of the amendments to the claims this rejection under §112, first paragraph should be withdrawn.

5) Claim Rejections under 35 USC §112, first paragraph

Claims 1-7, 31-45, 47, 50-52, 55-68, 85, 151-156 were rejected under 35 USC §112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner's basis of the rejection is that the amendment filed 2/5/2007 allegedly introduces new matter into the specification as originally filed because the claims have been amended to recite methods for treating any individual comprising administering a ligand for a pattern recognition receptor and exposing the subject to radiation. Examiner alleged that the originally filed specification and claims referred to the use of radiation only for the treatment of subjects with cancer. Thus the Examiner alleges that the amendment constitutes a broadening of the scope of the claims to a genus of methods that was not originally contemplated.

Applicants respectfully traverse the allegation; however, for business considerations and in an attempt to expedite prosecution the claims have been amended such that all the above rejected claims now read on methods of treating a subject having cancer comprising administering a ligand for a pattern recognition receptor and exposing the subject to radiation.

In light of the amendments to the claims the rejection under §112, first paragraph should be withdrawn.

6) Claim Rejections under 35 USC §102(b)

Claims 1-7, 9, 10, 31-33, 41, 52, 61, 63, 64, 85-87, 112-119, 121 and 151-155 were rejected under 35 USC §102(b) as being allegedly anticipated by Milas (Milas, L., Develop. Biol. Standard., 38:301-306, 1978) as evidenced by Hacker (Hacker, G. et al, Immunology, 105: 245-251, 2002, March).

The Examiner has summarized that Milas allegedly teaches a method that comprises intravenous administration of formalin-killed *C. parvum* diluted in solution A (8.0 NaCl, 0.4g KCl, 1.0g glucose and 0.35 g NaHCO₃ in 1 liter H₂O) and gamma-irradiation in mice bearing mammary tumors. Therefore, Milas teaches the method steps of administering a composition comprising a ligand (*C. Parvum*) with a delivery vehicle (solution A, which is non-liposomal) and also administering radiation.

Applicants have reviewed the Milas reference and the Examiner's rejection and respectfully traverses. However, for business consideration and in the interest of expediting prosecution all of the claims of the present invention now incorporate the use of a liposomal delivery vehicle. As the Examiner pointed out in his rejection above, the delivery vehicle disclosed by the Milas reference "(solution A, which is non-liposomal)" does not teach the use of a liposomal delivery vehicle and thus cannot anticipate claims with liposomal delivery vehicles.

Based on the amendments to all the rejected claims which now encompass a liposomal delivery vehicle the rejection under §102(b) should be withdrawn.

7) Claim Rejections under 35 USC §102(e)

Claims 1-7, 9, 10, 31-34, 41-45, 52, 61, 64, 65, 85-87, 112, 113, 118-121, 151 and 156 were rejected under 35 USC § 102(e) as being allegedly anticipated by Raz (US 6,534,062 issued Mar. 18, 2003; effective filing date is July 5, 2000).

Applicants have reviewed the Raz reference and the Examiner's rejection and respectfully traverses. However, for business considerations and in the interest of expediting prosecution all of the claims of the present invention now incorporate the liposomal embodiments found in previously non-rejected claim 37 comprising a liposome, wherein said liposome is a positively charged liposome, a negatively charged liposome, or a neutral liposome."

Because the Examiner agrees that Raz does not anticipate the elements of claim 37, the incorporation of the elements of claim 37 into the previously rejected claims should overcome the Examiner's rejection.

Therefore, Applicants respectfully request the rejection under §102(e) be withdrawn.

8) Claim Rejections under 35 USC §103(a) under Dow

Claims 1-5, 31-37, 39, 40, 43-44, 61, 64, 65, 85, 112, 118, 120, 151 and 156 were rejected under 35 USC 103(a) as allegedly being obvious over Dow (US 6,693,086) in view of Milas.

The Examiner agreed that the applied reference has a common inventor with the instant application. Applicants would like to thank the Examiner for pointing out that based on the earlier effective U.S. filing date of the reference, Dow constitutes prior art only under 35 USC § 102(e). Thus, this rejection under 35 USC § 103(a) could be overcome by a showing under 37 CFR § 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another".

Specifically and in response to the Examiner's rejection Steven Dow has declared that:

a) he is the inventor of the subject matter corresponding with claims 34-37 and column 6, lines 41-58 of the '086 patent which teaches methods for treating cancer comprising the administration of immunostimulatory nucleic acids complexed with liposomes;

b) he is the inventor of the subject matter corresponding with column 3, lines 8-25 of the '086 patent which teaches a method that can elicit a systemic, anti-tumor immune response in a mammal that results in an increase in effector cell activity and particularly natural killer cell activity and an increased production of interferon gamma;

c) he is the inventor of the subject matter corresponding with column 13, lines 14-29 of the '086 patent which teaches that the nucleic acid may be any nucleic acid, coding or non-coding, and not necessarily operatively linked to a transcription control sequence; and

d) he is the inventor of the subject matter corresponding with column 13, lines 34-35 of the '086 patent which teaches the use of a recombinant nucleic acid (reads on synthetic DNA).

Based on the included § 1.132 Declaration, the Dow reference was derived from the inventor of this application and is thus not an invention "by another" as is required under 35 USC § 103(a).

In light of the above, Applicants respectfully submit that this rejection be withdrawn.

9) Claim Rejections under 35 USC §103(a) under Davis and Milas

Claims 1-7, 9, 10, 31-33, 41, 42, 52, 61, 64, 65, 85-87, 112, 118, 119, 121, 151 and 156 were rejected under 35 USC §103(a) as being allegedly unpatentable over Davis (US 6,406,705; issued June 18, 2002, effective filing date June 3, 1999).

Applicants have reviewed the Davis and Milas references and the Examiner's rejection and respectfully traverses. However, for business considerations and in the interest of expediting prosecution all of the claims of the present invention now incorporate the liposomal embodiments found in previously non-rejected claim 37 comprising a liposome, wherein said liposome is a positively charged liposome; a negatively charged liposome; or a neutral liposome.

Because the Examiner has suggested that the elements of claim 37 are not obvious in light of the Davis and Milas references, the incorporation of the elements of claim 37 into the previously rejected claims should overcome the Examiner's rejection.

Therefore, Applicants respectfully request the above rejection under §103(a) be withdrawn.

10) Claim Rejections under 35 USC §103(a) under Maes and Raz

Claims 1-31 and 60-62 were rejected under 35 USC §103(a) as being allegedly unpatentable over Raz in view of Maes(US 3,725,545; issued Apr. 3, 1973).

Applicants have reviewed the Maes and Raz references and the Examiner's rejection and respectfully traverses. However, for business considerations and in the interest of expediting prosecution all of the claims of the present invention now incorporate the liposomal embodiments found in previously non-rejected claim 37 comprising a liposome, wherein said liposome is a positively charged liposome; a negatively charged liposome; or a neutral liposome.

Because the Examiner has suggested that the elements of claim 37 are not obvious in light of the Maes and Raz references, the incorporation of the elements of claim 37 into the previously rejected claims should overcome the Examiner's rejection.

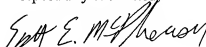
Therefore, Applicants respectfully request the above rejection under §103(a) be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 858-350-6100.

Respectfully submitted,



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